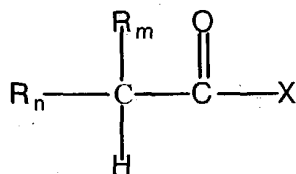


CLAIMS

What is claimed is:

1. A compound of Formula (I) or (II), or a pharmaceutically acceptable salt thereof;
wherein the compound of Formula (I) is:



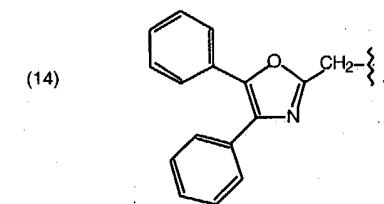
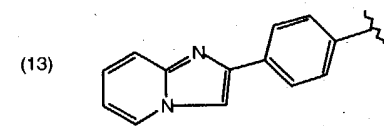
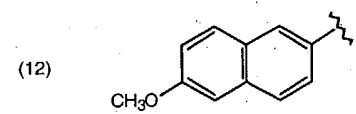
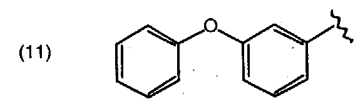
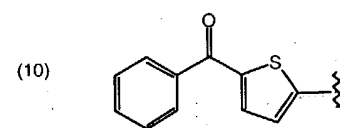
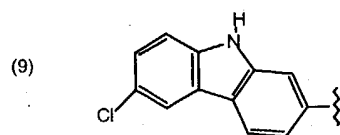
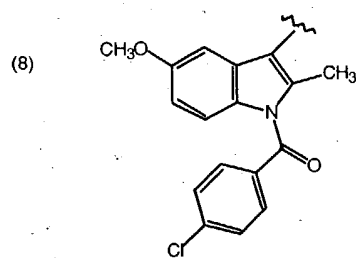
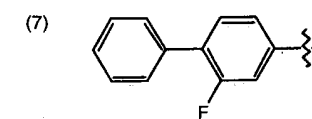
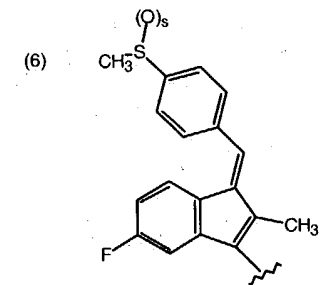
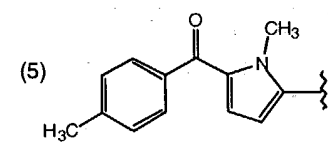
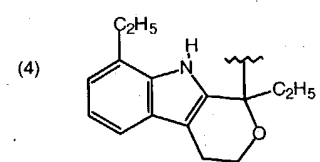
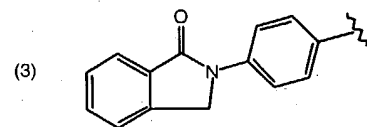
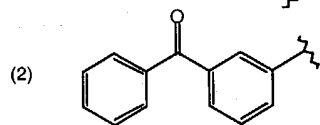
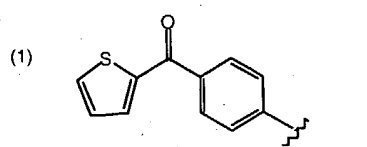
(I)

wherein:

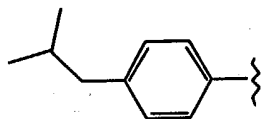
R_m is a hydrogen or a lower alkyl group;

R_n is:

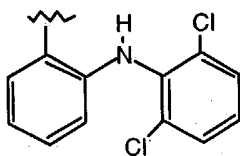
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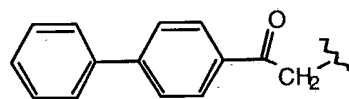
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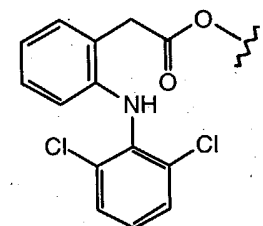
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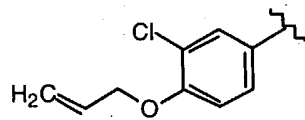
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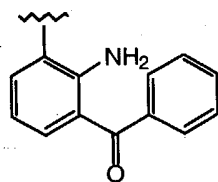
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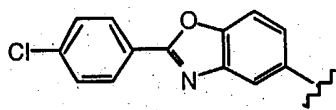
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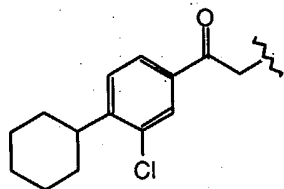
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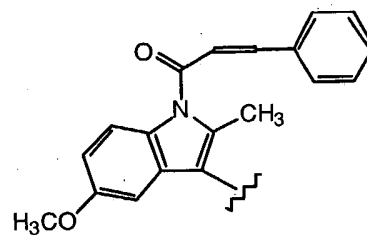
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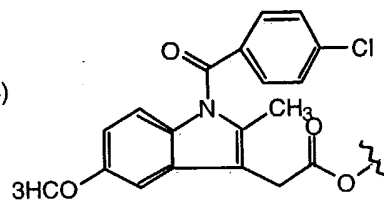
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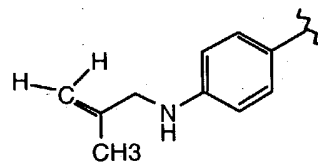
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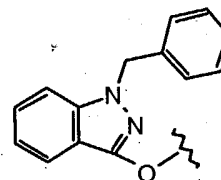
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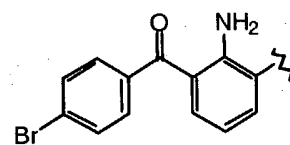
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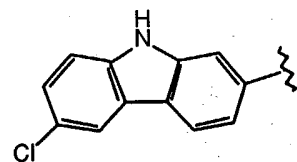
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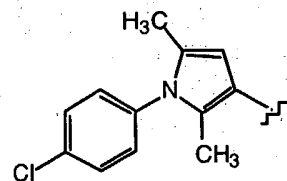
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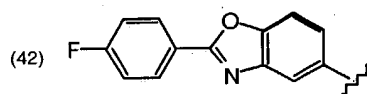
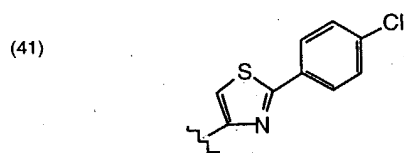
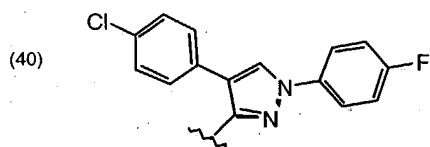
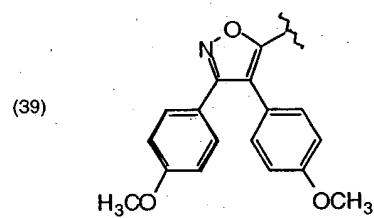
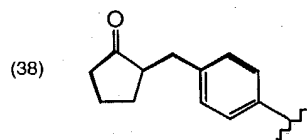
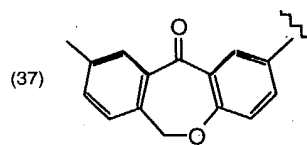
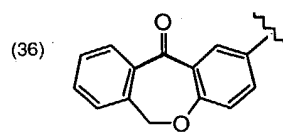
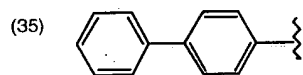
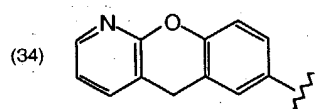
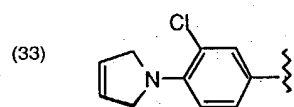
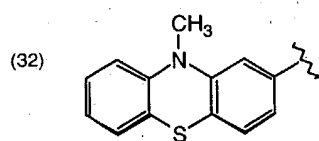
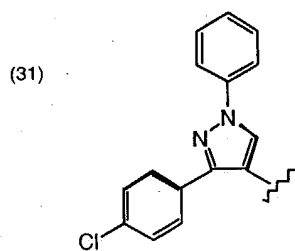
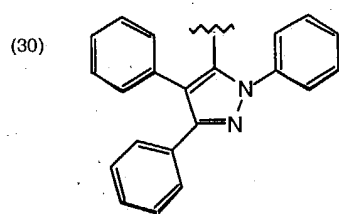


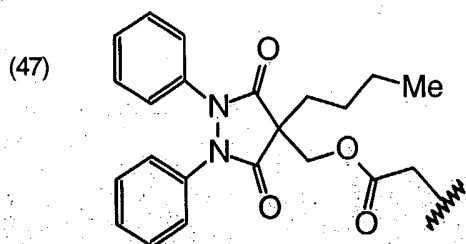
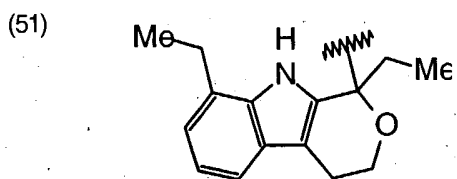
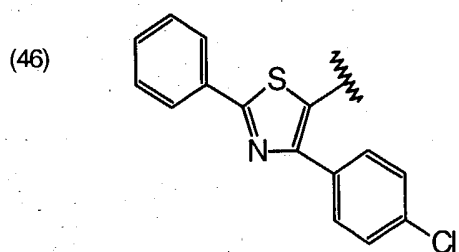
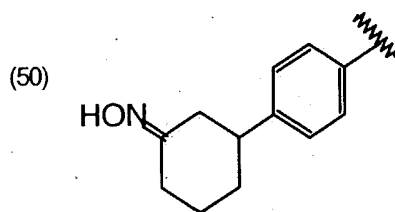
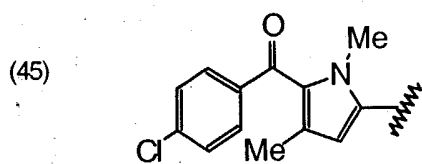
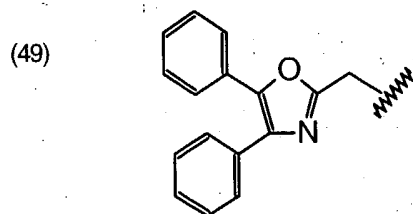
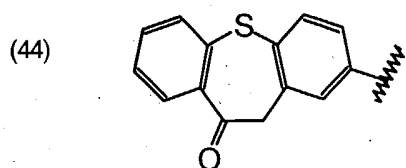
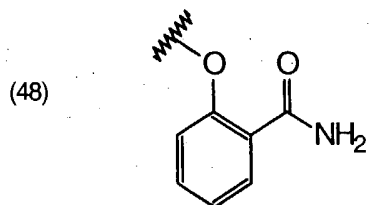
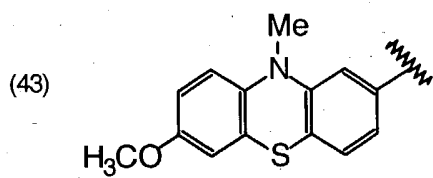
(28)



(29)

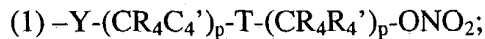




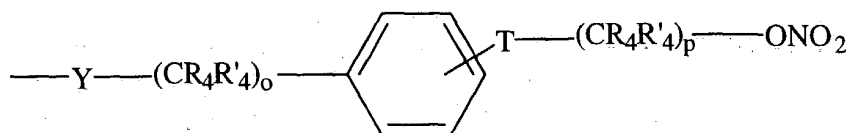


s is an integer of 0 or 1;

X is:



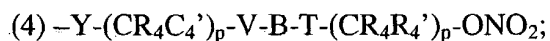
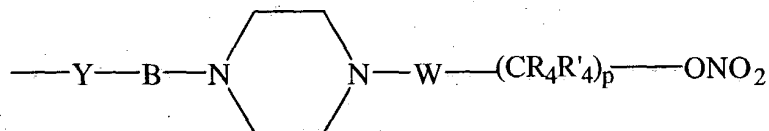
(2)



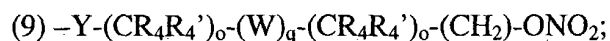
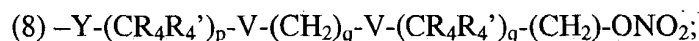
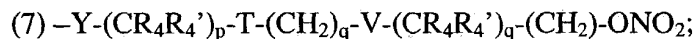
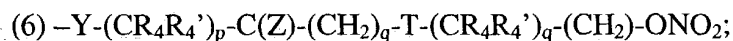
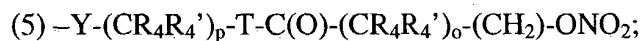
5

wherein T is ortho, meta or para;

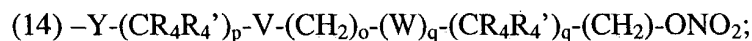
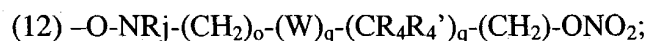
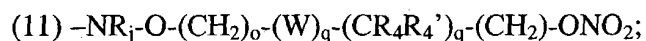
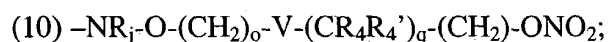
(3)



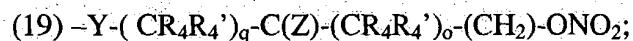
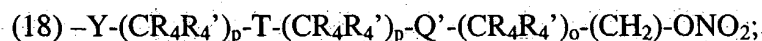
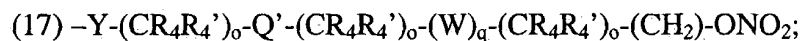
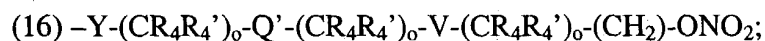
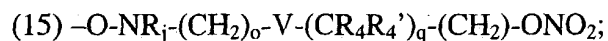
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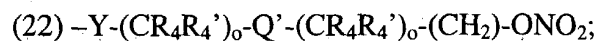
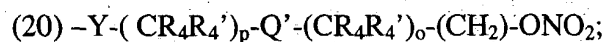
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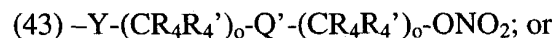
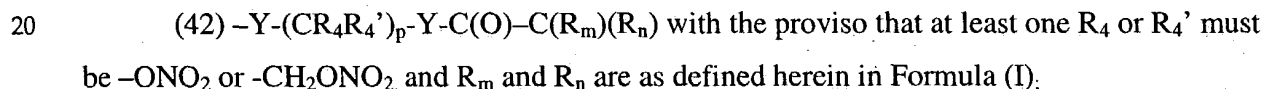
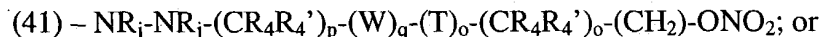
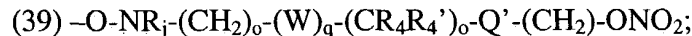
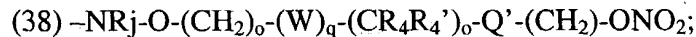
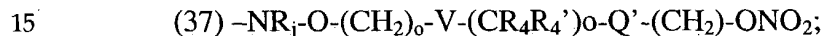
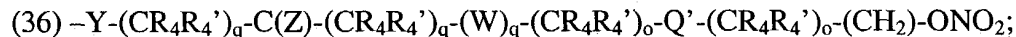
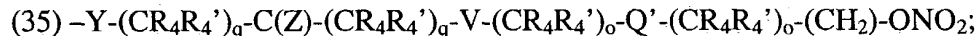
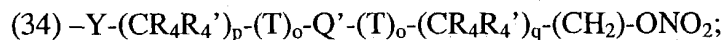
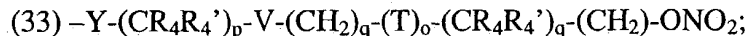
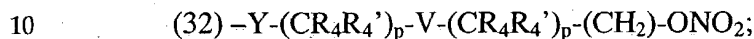
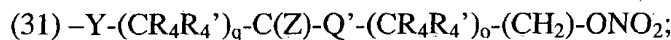
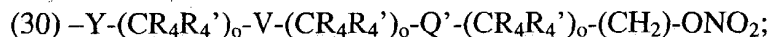
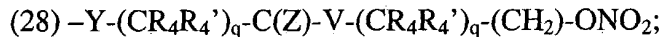
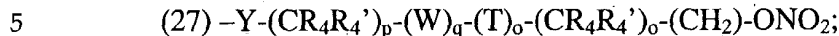
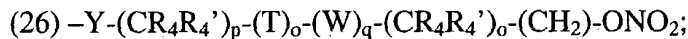
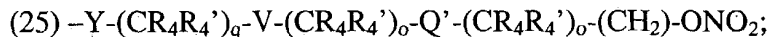
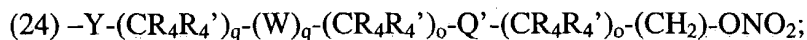
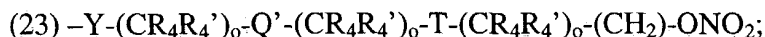


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25





R_4 and R_4' at each occurrence are independently a hydrogen, lower alkyl group, $-OH$,
25 $-CH_2OH$, $-ONO_2$, $-NO_2$ or $-CH_2ONO_2$; or R_4 and R_4' taken together with the carbon atom to which they are attached are a cycloalkyl group or a heterocyclic ring;

V is $-C(O)-T-$, $-T-C(O)-$, $-T-C(O)-T$ or $T-C(O)-C(O)-T$;

W is a covalent bond or a carbonyl group;

T at each occurrence is independently an oxygen, $(S(O)_o)_o$ or NR_j ;

30 R_j is a hydrogen, an alkyl group, an aryl group, a heterocyclic ring, an alkylcarbonyl group, an alkylaryl group, an alkylsulfinyl group, an alkylsulfonyl group, an arylsulfinyl group,

an arylsulfonyl group, a sulfonamido group, a N-alkylsulfonamido group, a N,N-diarylsulfonamido group, a N-arylsulfonamido group, a N-alkyl-N-arylsulfonamido group, a carboxamido group or a hydroxyl group;

p at each occurrence is independently an integer from 1 to 6;

q at each occurrence is independently an integer from 1 to 3;

o at each occurrence is independently an integer from 0 to 2;

Y is oxygen or sulfur (-S-);

B is either phenyl or $(CH_2)_o$;

Q' is a cycloalkyl group, a heterocyclic ring or an aryl group;

Z is $(=O)$, $(=N-OR_5)$, $(=N-NR_5R'_5)$ or $(=CR_5R'_5)$;

M and M' are each independently $-O^-H_3N^+-(CR_4R'_4)_q-CH_2ONO_2$ or $-T-(CR_4R'_4)_o-CH_2ONO_2$;

R_5 and R'_5 at each occurrence are independently a hydrogen, a hydroxyl group, an alkyl group, an aryl group, an alkylsulfonyl group, an arylsulfonyl group, a carboxylic ester, an alkylcarbonyl group, an arylcarbonyl group, a carboxamido group, an alkoxyalkyl group, an alkoxyaryl group, a cycloalkyl group or a heterocyclic ring; and

with the proviso that for X in the compounds of Formulas (I) and (II):

when Y is oxygen or sulfur in Formula 1, T is $-N(CH_3)$ and R_4 and R'_4 are hydrogen, p cannot be the integer 2;

when Y is oxygen or sulfur in Formula 1, and T is oxygen, at least one R_4 or R'_4 must be $-OH$, $-NO_2$ or $-CH_2ONO_2$ or R_4 and R'_4 taken together with the carbon atom to which they are attached are a cycloalkyl group or a heterocyclic ring;

when Y is oxygen or sulfur in Formula 9, and W is a covalent bond, at least one R_4 or R'_4 must be $-OH$, $-ONO_2$, $-NO_2$ or $-CH_2ONO_2$ or R_4 and R'_4 taken together with the carbon atom to which they are attached are a cycloalkyl group or a heterocyclic ring;

when Y is oxygen or sulfur in Formula 17, and W is a covalent bond, and R_4 and R'_4 are each independently a hydrogen or a lower alkyl group, Q' cannot be a phenyl group or a saturated, unsaturated or aromatic heterocyclic ring having 5 or 6 atoms, containing one to three heteroatoms, wherein the heteroatoms are each independently nitrogen, oxygen or sulfur;

when Y is oxygen in Formula 17, and W is a covalent bond, and R_4 and R'_4 are hydrogen, Q' cannot be a cycloalkyl group;

when Y is oxygen or sulfur in Formula 20, 22 or 43, and R₄ and R₄' are each independently a hydrogen or a lower alkyl group, Q' cannot be a phenyl group or a saturated, unsaturated or aromatic heterocyclic ring having 5 or 6 atoms, containing one to three

5 heteroatoms, wherein the heteroatoms are each independently nitrogen, oxygen or sulfur;

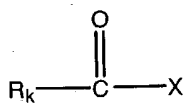
when Y is oxygen in Formula 20, 22 or 43, and W is a covalent bond, and R₄ and R₄' are hydrogen, Q' cannot be a cycloalkyl group;

when Y is oxygen or sulfur in Formula 26 or 27, T is -N(CH₃), W is a covalent bond and R₄ and R₄' are hydrogen, p cannot be the integer 2, and o cannot be the integer 1 in -(CR₄R₄')_o;

10 when Y is oxygen or sulfur in Formula 26 or 27, W is a covalent bond, T is oxygen and o is the integer 1, at least one R₄ or R₄' must be -OH, -NO₂ or -CH₂ONO₂ or R₄ and R₄' taken together with the carbon atom to which they are attached are a cycloalkyl group or a heterocyclic ring; and

with the further proviso that the the compounds of Formula (I), do not include the
15 compounds of ACS registry numbers 502158-05-6, 410071-57-7, 311336-65-9, 311336-63-7, 311336-62-6, 290335-27-2, 290335-26-1, 290335-25-0, 174454-51-4, 170591-17-0, 163133-43-5; 497818-55-0, 454170-89-9, 326850-43-5, 311336-66-0, 311336-64-8, 311336-61-5, 290335-37-4, 290335-36-3, 290335-35-2, 183195-09-7, 183195-07-5, 183195-06-4, 183195-04-2, 174454-43-4, 156661-01-7; 301838-28-8, 290335-34-1, 290335-33-0, 290335-32-9, 290335-31-
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25 189282-77-7, 189282-76-6, 188209-49-9, 174454-50-3, 174454-47-8, 158836-71-6, 156970-87-5, 156970-86-4, and 156970-83-1;

wherein the compound of Formula (II) is:

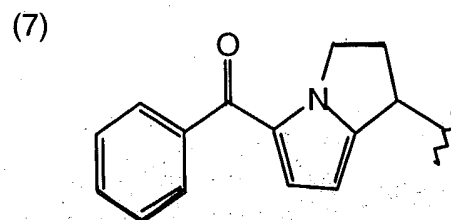
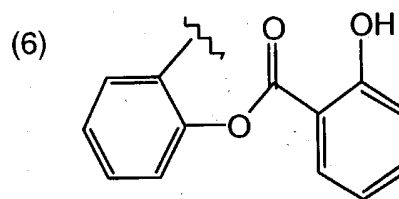
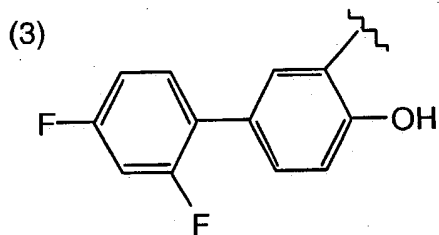
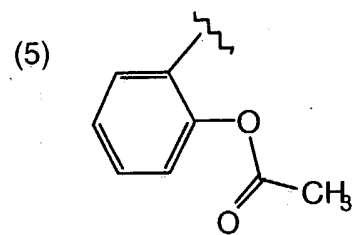
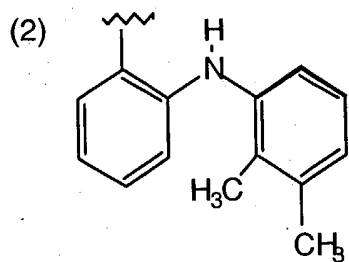
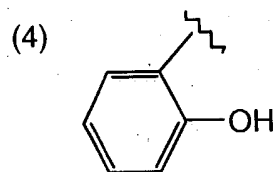
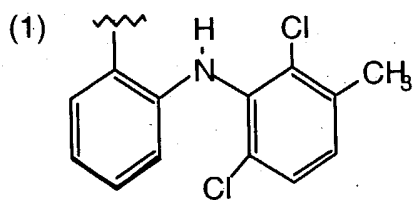


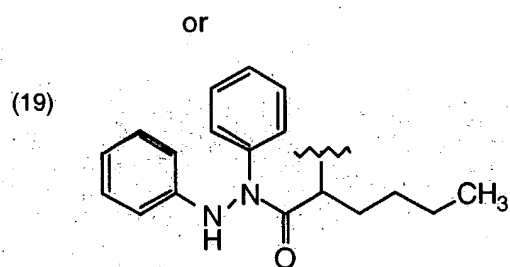
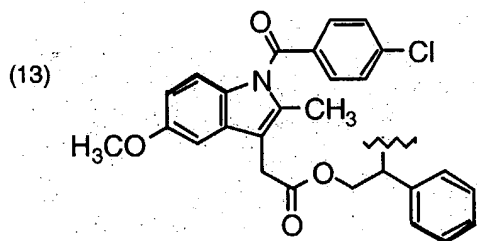
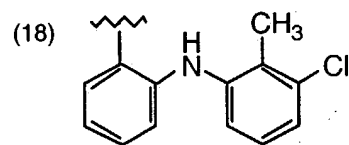
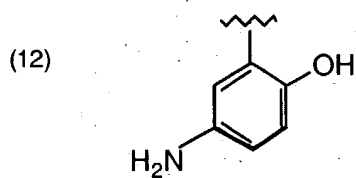
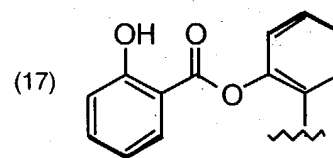
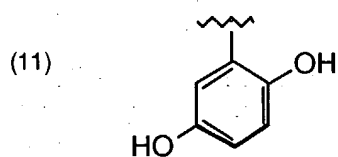
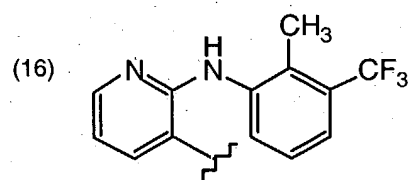
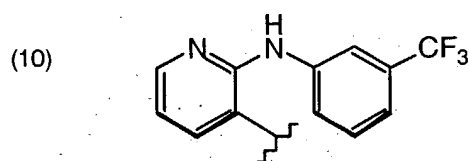
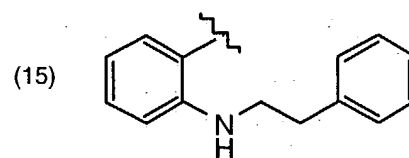
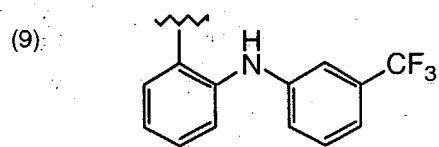
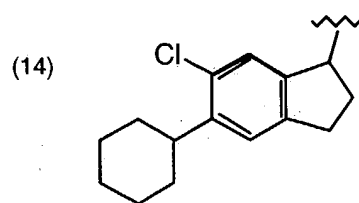
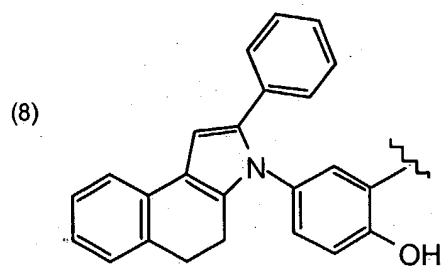
(II)

wherein:

R_k is:

5





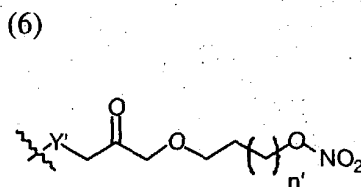
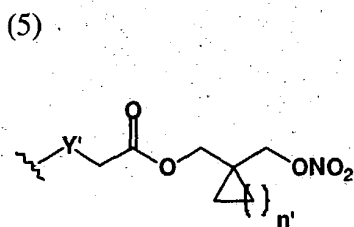
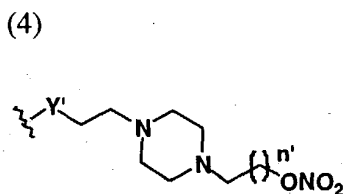
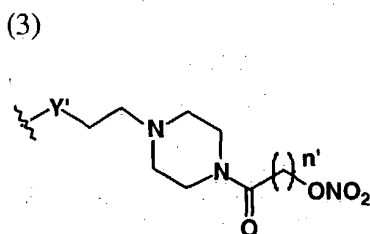
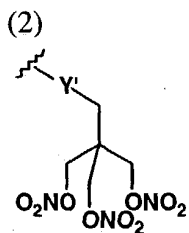
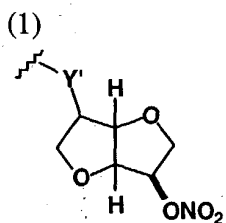
and X is as defined herein in Formula (I) or

(45) $-Y-(CR_4R_4')_p-Y-C(O)-R_k$ with the proviso that at least one R_4 or R_4' must be $-ONO_2$ or $-CH_2ONO_2$, and R_k is as defined herein in Formula (II); and

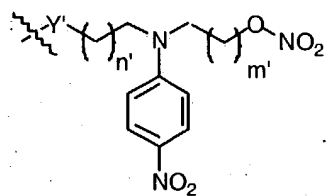
with the proviso that the compounds of Formula (II) do not include the compound of ACS
 5 registry numbers 410071-45-3, 410071-44-2, 410071-40-8, 410071-39-5, 410071-38-4, 410071-
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 287118-96-1, 206556-93-6, 190442-14-9, 190442-13-8, 190442-12-7, 190442-12-7, 190442-11-
 6, 188025-64-1, 184644-94-8, 184644-92-6, 184644-90-4, 177598-18-4, 177598-17-3, 177598-
 13-9, 177598-12-8, 175033-36-0, 171781-26-3, 154424-73-4, 145585-70-2, 140218-52-6 and
 10 140218-49-1; 478163-51-8, 410071-48-6, 410071-47-5, 410071-46-4, 410071-43-1, 410071-42-
 0, 410071-41-9, 410071-37-3, 410071-36-2, 410071-35-1, 410071-34-0, 410071-33-9, 401916-
 64-1, 302606-04-8, 257626-09-8, 257626-08-7, 256499-26-0, 209002-97-9, 204268-65-5,
 203563-95-5, 177598-09-3, 164790-48-1 and 163385-76-0.

2. A composition comprising the compound of claim 1 and a pharmaceutically
 15 acceptable carrier.

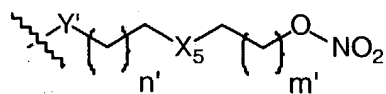
3. The compound of claim 1, wherein X is:



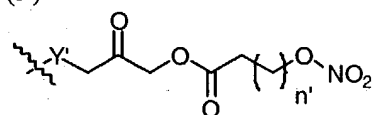
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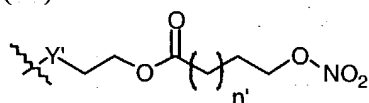
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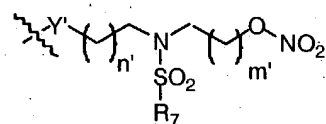
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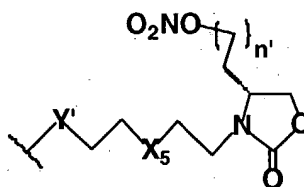
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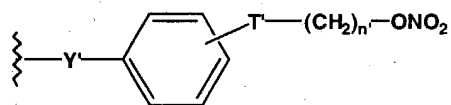
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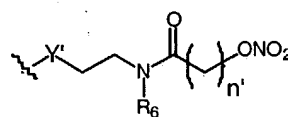
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(13)

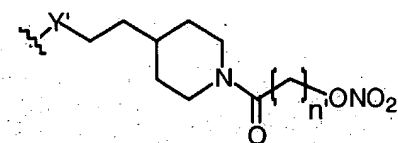


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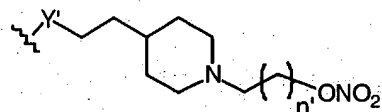


wherein T' maybe ortho, meta or para

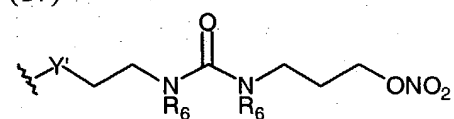
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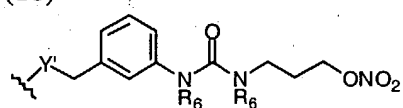
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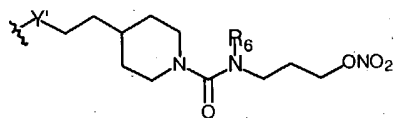
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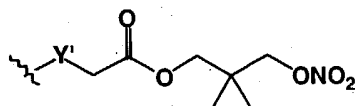
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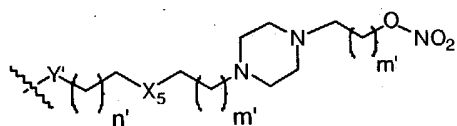
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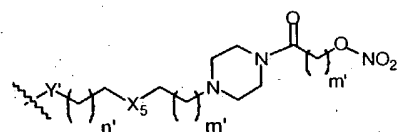
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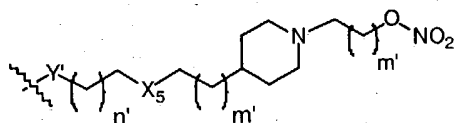
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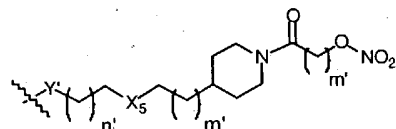
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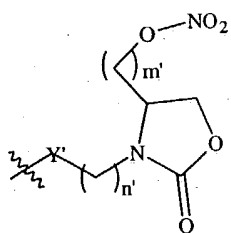
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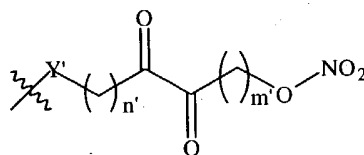
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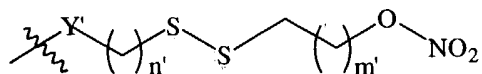
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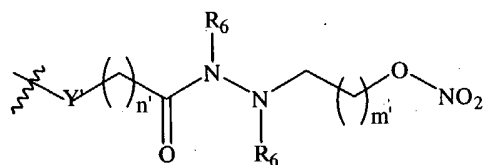
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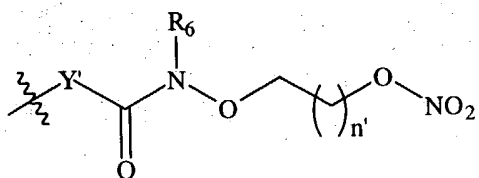
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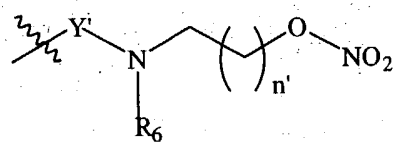
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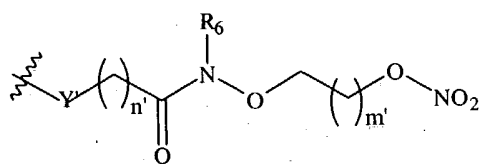
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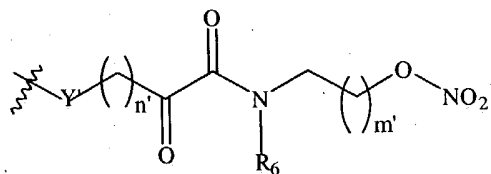
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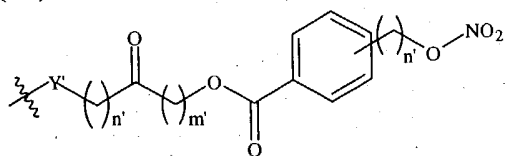
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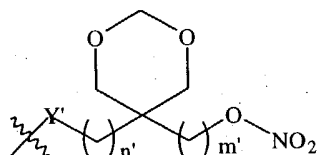
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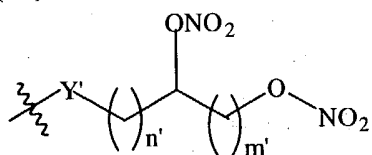
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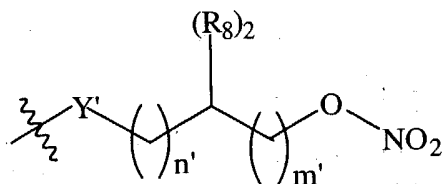
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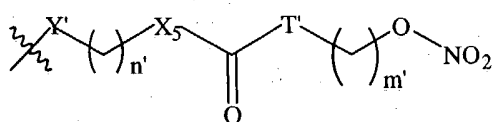
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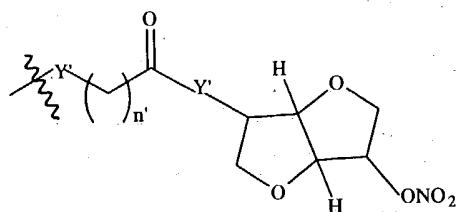
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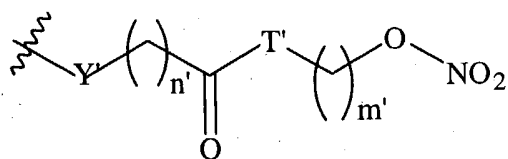
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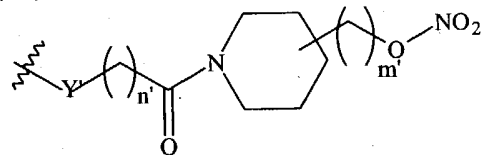
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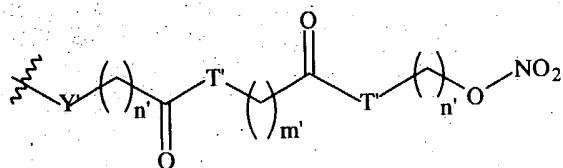
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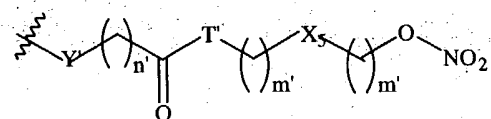
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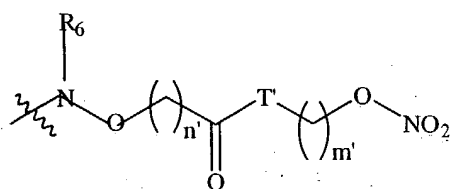


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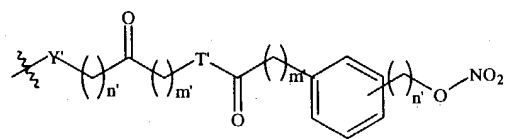
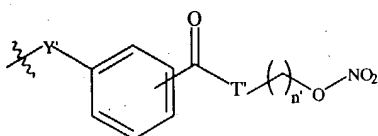


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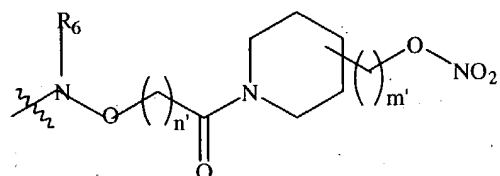
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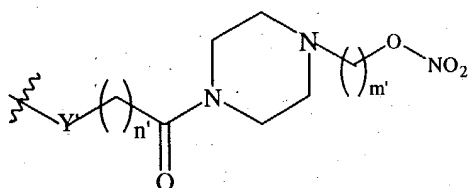
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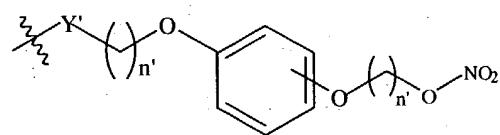
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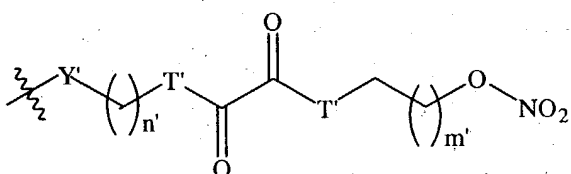
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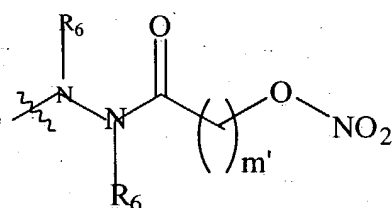
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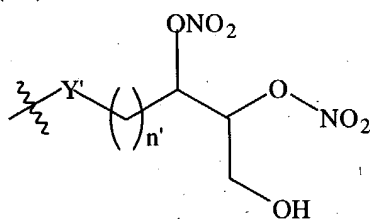
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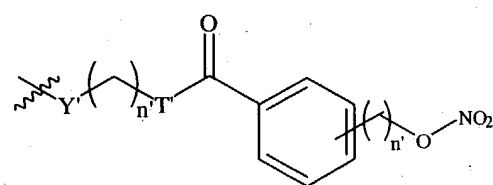
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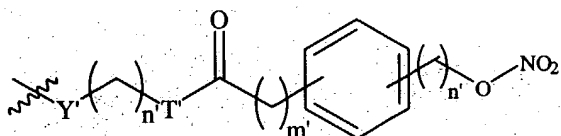
(51)



(52)



(53)



wherein:

Y' is oxygen or sulfur;

T' is oxygen, sulfur or NR₆;

X₅ is oxygen, (S(O)_o)_o or NR₆;

R₆ is a hydrogen, a lower alkyl group, an aryl group;

R₇ is a lower alkyl group or an aryl group;

5 R₈ at each occurrence is independently is a hydrogen, a hydroxyl group, a lower alkyl group, an aryl group, -NO₂, -CH₂-ONO₂ or -CH₂-OH;

n' and m' are each independently an integer from 0 to 10;

o is as defined herein; and

with the proviso for Formula 8 for X:

10 Y' and X₅ cannot be oxygen; and

when Y' is oxygen and X₅ is -N(CH₃), then n' and m' must be any integer except 1.

4. The compound of claim 1, wherein the compound of Formula (I) is a nitrosated acemetacin, a nitrosated aceclofenac, a nitrosated alminoprofen, a nitrosated amfenac, a nitrosated bendazac, a nitrosated benoxaprofen, a nitrosated bromfenac, a nitrosated bucloxic acid, a nitrosated butibufen, a nitrosated carprofen, a nitrosated cinmetacin, a nitrosated clopirac, a nitrosated diclofenac, a nitrosated etodolac, a nitrosated felbinac, a nitrosated fenclozic acid, a nitrosated fenbufen, a nitrosated fenoprofen, a nitrosated fentiazac, a nitrosated flunoxaprofen, a nitrosated flurbiprofen, a nitrosated ibufenac, a nitrosated ibuprofen, a nitrosated indomethacin, a nitrosated isofezolac, a nitrosated isoxepac, a nitrosated indoprofen, a nitrosated ketoprofen, a nitrosated lonazolac, a nitrosated loxoprofen, a nitrosated metiazinic acid, a nitrosated mofezolac, a nitrosated mioprofen, a nitrosated naproxen, a nitrosated oxaprozin, a nitrosated pirozolac, a nitrosated pirprofen, a nitrosated pranoprofen, a nitrosated protizinic acid, a nitrosated salicylamide, a nitrosated sulindac, a nitrosated suprofen, a nitrosated suxibuzone, a nitrosated tiaprofenic acid, a nitrosated tolmetin, a nitrosated xenbucin, a nitrosated ximoprofen, a nitrosated zaltoprofen a nitrosated zomepirac; the compound of Formula II is a nitrosated aspirin, a nitrosated acemetcin, a nitrosated bumadizon, a nitrosated carprofenac, a nitrosated clidanac, a nitrosated diflunisal, a nitrosated enfenamic acid, a nitrosated fendosal, a nitrosated flufenamic acid, a nitrosated flunixin, a nitrosated gentisic acid, a nitrosated ketorolac, a nitrosated meclofenamic acid, a nitrosated mefenamic acid, a nitrosated mesalamine, a nitrosated niflumic acid, a nitrosated salsalate, a nitrosated tolfenamic acid or a nitrosated tropensin.

5. A method for treating or reducing inflammation, pain or fever in a patient in need

thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

6 A method for treating a gastrointestinal disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

7. The method of claim 6, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, constipation, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

8. A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

9. The method of claim 8, wherein the wound is an ulcer.

10. A method for treating or reversing gastrointestinal, renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

11. A method for treating an inflammatory disease in patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

12. The method of claim 11, wherein the inflammatory disease is a cardiovascular disorder, reperfusion injury to an ischemic organ, angiogenesis, arthritis, asthma, bronchitis, premature labor, tendinitis, bursitis, an autoimmune disease, an immunological disorder, a skin-related condition, neoplasia, an inflammatory process in a disease, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, a microbial infection, a bacterial-induced inflammation, a viral induced inflammation, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, a sexual dysfunction or activation, adhesion and infiltration of neutrophils at the site of inflammation.

13. The method of claim 12, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an

adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamous cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

14. The method of claim 12, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia, senile dementia, memory loss or central nervous system damage resulting from stroke, ischemia or trauma.

15. A method for treating an ophthalmic disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

16. The composition of claim 2, further comprising at least one therapeutic agent.

17. The composition of claim 16, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a cyclooxygenase inhibitor, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor, a H₂ antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

18. A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 16.

19. A method for treating a gastrointestinal disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 16.

20. The method of claim 19, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, constipation, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia,

gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

21. A method for facilitating wound healing in a patient in need thereof comprising
5 administering to the patient a therapeutically effective amount of the composition of claim 16.

22. The method of claim 21, wherein the wound is an ulcer.

23. A method for treating or reversing gastrointestinal, renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 16.

10 24. A method for for treating an inflammatory disease in patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 16.

25. The method of claim 24, wherein the inflammatory disease is a cardiovascular disorder, reperfusion injury to an ischemic organ, angiogenesis, arthritis, asthma, bronchitis,
15 premature labor, tendinitis, bursitis, an autoimmune disease, an immunological disorder, a skin-related condition, neoplasia, an inflammatory process in a disease, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, a microbial infection, a bacterial-induced inflammation, a viral induced inflammation, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue
20 deterioration, a sexual dysfunction or activation, adhesion and infiltration of neutrophils at the site of inflammation.

26. The method of claim 25, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a
25 small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamous cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

30 27. The method of claim 25, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia,

alcoholic dementia, senile dementia, memory loss or central nervous system damage resulting from stroke, ischemia or trauma.

28. A method for treating an ophthalmic disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 16.

29. A composition comprising at least one compound of claim 1 and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.

30. The composition of claim 29, further comprising a pharmaceutically acceptable carrier.

31. The composition of claim 29, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.

32. The composition of claim 31, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione, or S-nitroso-cysteinyl-glycine.

33. The composition of claim 31, wherein the S-nitrosothiol is:

(i) $\text{HS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{SNO}$;

(ii) $\text{ONS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{R}_e$; or

(iii) $\text{H}_2\text{N}-\text{CH}(\text{CO}_2\text{H})-(\text{CH}_2)_m-\text{C}(\text{O})\text{NH}-\text{CH}(\text{CH}_2\text{SNO})-\text{C}(\text{O})\text{NH}-\text{CH}_2-\text{CO}_2\text{H}$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylaryl amino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl,

an arylsulfonyloxy, a urea, a nitro, -T-Q-, or $-(C(R_g)(R_h))_k-T-Q$ or R_e and R_f taken together are an oxo, a thial, a heterocyclic ring, a cycloalkyl group, an oxime, a hydrazone or a bridged cycloalkyl group; Q is -NO or -NO₂; and T is independently a covalent bond, a carbonyl, an oxygen, -S(O)_o- or -N(R_a)R_i-, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyloxy, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, -CH₂-C(T-Q)(R_g)(R_h), or $-(N_2O_2)^- \cdot M^+$, wherein M⁺ is an organic or inorganic cation; with the proviso that when R_i is -CH₂-C(T-Q)(R_g)(R_h) or $-(N_2O_2)^- \cdot M^+$; then "-T-Q" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group; and R_g and R_h at each occurrence are independently R_e.

34. The composition of claim 29, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, nitrosated L-homoarginine, nitrosylated L-homoarginine), citrulline, ornithine, glutamine, lysine, an arginase inhibitor or a nitric oxide mediator.

35. The composition of claim 29, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:

- (i) a compound that comprises at least one ON-O- or ON-N- group;
- (ii) a compound that comprises at least one O₂N-O-, O₂N-N- or O₂N-S- or group;
- (iii) a N-oxo-N-nitrosoamine having the formula: R^{1''} R^{2''} N-N(O-M⁺)-NO, wherein R^{1''} and R^{2''} are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M⁺ is an organic or inorganic cation.

36. The composition of claim 35, wherein the compound comprising at least one

ON-O- or ON-N- group is an ON-O-polypeptide, an ON-N-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, an ON-O-heterocyclic compound or an ON-N-heterocyclic compound.

37. The composition of claim 35, wherein compound comprising at least one O₂N-O-, O₂N-N- or O₂N-S- group is an O₂N-O-polypeptide, an O₂N-N-polypeptide, an O₂N-S-polypeptide, an O₂N-O-amino acid, O₂N-N-amino acid, O₂N-S-amino acid, an O₂N-O-sugar, an O₂N-N-sugar, O₂N-S-sugar, an O₂N-O-oligonucleotide, an O₂N-N-oligonucleotide, an O₂N-S-oligonucleotide, , a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-S-hydrocarbon, an O₂N-O-heterocyclic compound, an O₂N-N-heterocyclic compound or an O₂N-S-heterocyclic compound.

38. The composition of claim 29, further comprising at least one therapeutic agent.

39. The composition of claim 38, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a cyclooxygenase-2 inhibitor, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a HMG CoA inhibitor, a H₂ antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

40. A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 38.

41. A method for treating a gastrointestinal disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 38.

42. The method of claim 41, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, constipation, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

43. A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 38.

44. The method of claim 43, wherein the wound is an ulcer.

45. A method for treating or reversing gastrointestinal, renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 38.

46. A method for treating inflammatory disease in patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 38.

47. The method of claim 46, wherein the inflammatory disease is a cardiovascular disorder, reperfusion injury to an ischemic organ, angiogenesis, arthritis, asthma, bronchitis, premature labor, tendinitis, bursitis, an autoimmune disease, an immunological disorder, a skin-related condition, neoplasia, an inflammatory process in a disease, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, a microbial infection, a bacterial-induced inflammation, a viral induced inflammation, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, a sexual dysfunction or activation, adhesion and infiltration of neutrophils at the site of inflammation.

48. The method of claim 47, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamous cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous

tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

49. The method of claim 47, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia,
5 alcoholic dementia, senile dementia, memory loss or central nervous system damage resulting from stroke, ischemia or trauma.

50. A method for treating an ophthalmic disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 29 or 38.

10 51. A kit comprising at least one compound of claim 1.

52. The kit of claim 51, further comprising (i) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; (ii) at least one therapeutic agent; or (iii) at least one compound that donates, transfers or releases nitric oxide,
15 induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent.

53. The kit of claim 52, wherein the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; the at least one therapeutic agent; or the
20 at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent; are in the form of separate components in the kit

54. A kit comprising the composition of claim 16, 29 or 38.

55. A compound selected from the group consisting of

25 2-(2-(nitrooxy)ethylthio)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
2-((2-(nitrooxy)ethyl)sulfonyl)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
2-((2-(nitrooxy)ethyl)sulfinyl)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
2-((2-(nitrooxy)ethyl)4-nitrophenyl)amino)ethyl 2-(6-methoxy-2-naphthyl)propanoate;
2R)-2,3-bis(nitrooxy)propyl(2S)-2(6-methoxy(2-naphthyl))propanoate;
30 (2R)-7-(nitrooxy)-4,8-dioxabicyclo(3.3.0)oct-2-yl(2S)-2-(6-methoxy (2-naphthyl)) propanoate;
phosphonomethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate 3-(nitrooxy) propylamine nitric

acid salt;

phosphonomethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate 4-nitro-1-(nitrooxy)-2-

((nitrooxy)methyl)but-2-ylamine salt;

(5-((nitrooxy)methyl-1,3-dioxan-5-yl)methyl (2S)-2-(6-methoxy(2-naphthyl))-propanoate;

5 2,2-bis(nitrooxy)propyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

3-(4-((nitrooxy)methyl)phenylcarbonyloxy)-2-oxopropyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

2-methyl-2-nitro-3-(nitrooxy)propyl(2S)-2-(6-methoxy(2-naphthyl)) propanoate;

2-nitro-3-(nitrooxy)-2-((nitrooxy)methyl)propyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

2-(N-(2-(nitrooxy)ethyl)carbamoyloxy)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

10 3-(2-(nitrooxy)ethoxy)phenyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

4-(2-(nitrooxy)ethoxy)phenyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

(N-methyl-N-(2-(nitrooxy)ethyl)carbamoyl)methyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

(N-ethyl-N-(2-(nitrooxy)ethyl)carbamoyl)methyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

2-(4-((nitrooxy)methyl)piperidyl)-2-oxoethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

15 (N-methyl-N-(((2-(nitrooxy)ethyl)oxycarbonyl)methyl)carbamoyl)methyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

(N-methyl-N-(((3-(nitrooxy)propyl)oxycarbonyl)methyl)carbamoyl)methyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

(N-methyl-N-((N-(2-(nitrooxy)ethyl)carbamoyl)methyl)carbamoyl)methyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

20 naphthyl))propanoate;

((2-(nitrooxy)ethyl)oxycarbonyl)methyl 2-(6-methoxy-2-naphthyl)propanoate;

(N-(3-(nitrooxy)propyl)carbamoyl)methyl 2-(6-methoxy-2-naphthyl)propanoate;

((2-((2-(nitrooxy)ethyl)sulfonyl)ethyl)oxycarbonyl)methyl 2-(6-methoxy-2-naphthyl)propanoate;

1S, 5S, 2R, 6R)-6-(nitrooxy)-4,8-dioxabicyclo(3.3.0)oct-2-yl)oxycarbonyl) methyl (2S)-2-(6-

25 methoxy (2-naphthyl)) propanoate;

(2S)-2,3-bis(nitrooxy)propyl(2S)-2-(6-methoxy-5-nitro(2-naphthyl)) propanoate;

2S)-2-hydroxy-3-(nitrooxy)propyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

(2R)-2-hydroxy-3-(nitrooxy)propyl (2S)-2-(6-methoxy(2-naphthyl)) propanoate;

(2S)-2-(6-methoxy(2-naphthyl))-N-((N-(2-(nitrooxy)ethyl)carbamoyl) methoxy)propanamide;

30 3-(2-(4-((nitrooxy)methyl)phenyl)acetyloxy)-2-oxopropyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;

- 2-(4-(2-(nitrooxy)ethyl)piperidyl)-2-oxoethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 4-((2-(nitrooxy)ethyl)oxycarbonyl)phenyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 2-((2-(nitrooxy)ethyl)oxycarbonyl)phenyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 (N-methyl-N-(3-(nitrooxy)propyl)carbamoyl)methyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 5 (2S)-2-(6-methoxy(2-naphthyl))-N-(2-(4-((nitrooxy)methyl)piperidyl)-2-oxoethoxy)propanamide;
 3-((2-(nitrooxy)ethyl)oxycarbonyl)phenyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 2-(4-(2-(nitrooxy)ethyl)piperazinyl)-2-oxoethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate
 hydrogen chloride;
 10 3-((2S)-2-(6-methoxy(2-naphthyl))propanoyloxy)-2-methyl-2-((nitrooxy)methyl)propyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 2-(4-(2-(nitrooxy)ethoxy)phenoxy)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 2-((2S)-2-(6-methoxy(2-naphthyl))propanoyloxy)ethyl 3-(nitrooxy)-propyl ethane-1,2-dioate;
 N-((2S)-2-(6-methoxy(2-naphthyl))propanoylamino)-4 (nitrooxy)butanamide;
 15 4-((2S)-2-(6-methoxy(2-naphthyl))propanoyloxy)(2S,3S)-2,3-bis(nitrooxy)butyl (2S)-2-(6-methoxy(2-naphthyl))propanoate
 (2S,3S)-2,3-bis(nitrooxy)-4-hydroxybutyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 2-((3-((nitrooxy)methyl)phenyl)carbonylamino)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 (2R)-2-(nitrooxy)-3-(phenylmethoxy)propyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 20 2-(N-methyl(4-((nitrooxy)methyl)phenyl)carbonylamino)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 (1S,2S,5S,6R)-6-(nitrooxy)-4,8-dioxabicyclo(3.3.0)oct-2-yl 2-(1-((4-chlorophenyl)carbonyl)-5-methoxy-2-methylindol-3-yl)acetate;
 (1S,2S,5S,6R)-6-(nitrooxy)-4,8-dioxabicyclo(3.3.0)oct-2-yl 2-(2-((2,6-
 25 dichlorophenyl)amino)phenyl)acetate;
 2-(((4-methylphenyl)sulfonyl)(2-(nitrooxy)ethyl)amino)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 2-(N-methyl-2-(4-((nitrooxy)methyl)phenyl)acetylamino)ethyl (2S)-2-(6-methoxy(2-naphthyl))propanoate;
 30 (2R)-2,3-bis(nitrooxy)propyl 2-(1-((4-chlorophenyl)carbonyl)-5-methoxy-2-methylindol-3-yl)acetate;

(2S)-2,3-bis(nitrooxy)propyl 2-(1-((4-chlorophenyl)carbonyl)-5-methoxy-2-methylindol-3-yl)acetate;

(2S)-2,3-bis(nitrooxy)propyl 2-(2-((2,6-dichlorophenyl)amino)phenyl)acetate;

(2R)-2,3-bis(nitrooxy)propyl 2-(2-((2,6-dichlorophenyl)amino)phenyl)acetate;

5 (2S)-2-(6-methoxy(2-naphthyl))-1-(4-(nitrooxy)butylthio)propan-1-one;

(N-methyl-N-(2-(nitrooxy)ethyl)carbamoyl)methyl 2-(1-((4-chlorophenyl)carbonyl)-5-methoxy-2-methylindol-3-yl)acetate;

(N-(2-(nitrooxy)ethyl)carbamoyl)methyl 2-(1-((4-chlorophenyl)carbonyl)-5-methoxy-2-methylindol-3-yl)acetate;

10 (N-(2-(nitrooxy)ethyl)carbamoyl)methyl 2-(2-((2,6-dichlorophenyl) amino)phenyl)acetate;
or a pharmaceutically acceptable salt thereof.

56. A composition comprising at least one compound of claim 55 and a pharmaceutically acceptable carrier.

57. The composition of claim 56, further comprising (i) at least one compound that
15 donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; (ii) at least one therapeutic agent; or (iii) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent.

20 58. A kit comprising at least one compound of claim 55.